

WHAT IS CLAIMED IS:

1. A stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein said calibrator or control has a pH of from about 4.0 to about 6.5.

2. The calibrator or control of claim 1, wherein said calibrator or control has a pH of from about 5.0 to about 6.0.

3. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one human synthetic natriuretic peptide.

4. The calibrator or control of claim 3, wherein said human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

5. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

6. The calibrator or control of claim 5, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

7. The calibrator or control of claim 5, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

8. The calibrator or control of claim 5, wherein the base is sodium hydroxide.

9. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one diluent.

10. The calibrator or control of claim 9, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

11. The calibrator or control of claim 10, wherein said natriuretic stabilizing compound is a protein or a polymer.

12. The calibrator or control of claim 11, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

13. The calibrator or control of claim 11, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

14. The calibrator or control of claim 9, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

15. The calibrator or control of claim 14, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

16. The calibrator or control of claim 14, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

17. The calibrator or control of claim 14, wherein the base is sodium hydroxide.

18. The calibrator or control of claim 1, wherein said calibrator or control can be stored at a temperature of from about 2 to about 8°C.

19. The calibrator or control of claim 1, wherein said calibrator or control can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

5 20. A stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein said calibrator or control comprises:

at least one diluent; and

at least one human synthetic natriuretic peptide,

10 wherein said calibrator or control has a pH of from about 4.0 to about 6.5.

21. The calibrator or control of claim 20, wherein said calibrator or control has a pH of from about 5.0 to about 6.0.

15 22. The calibrator or control of claim 20, wherein the human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

20 23. The calibrator or control of claim 20, wherein said calibrator or control further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

25 24. The calibrator or control of claim 23, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

25 25. The calibrator or control of claim 23, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

30 26. The calibrator or control of claim 23, wherein the base is sodium hydroxide.

27. The calibrator or control of claim 20, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

5 28. The calibrator or control of claim 27, wherein said natriuretic stabilizing compound is a protein or a polymer.

29. The calibrator or control of claim 28, wherein the protein is bovine serum albumin, a bovine gamma globulin, or a non-fat dry milk.

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30. The calibrator or control of claim 28, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

31. The calibrator or control of claim 27, wherein the diluent further  
15 comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

32. The calibrator or control of claim 31, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

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33. The calibrator or control of claim 31, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

34. The calibrator or control of claim 31, wherein the base is sodium  
25 hydroxide.

35. The calibrator or control of claim 20, wherein said calibrator or control can be stored at a temperature of from about 2 to about 8°C.

36. The calibrator or control of claim 20, wherein said calibrator or control can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

5 37. A method of making a stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein the method comprises the steps of:

a. mixing at least one diluent with at least one human synthetic natriuretic peptide to form a liquid calibrator or control;

10 b. measuring the pH of the liquid calibrator or control; and

c. depending upon the pH of the liquid calibrator or control measured in step b), adjusting the pH of the liquid calibrator or control to a pH of from about 4.0 to about 6.5.

15 38. The method of claim 37, wherein the pH of the liquid calibrator or control is adjusted to a pH of from about 5.0 to about 6.0.

20 39. The method of claim 37, wherein the human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

25 40. The method of claim 37, wherein the pH of the liquid calibrator or control is adjusted with at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

41. The method of claim 40, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

30 42. The method of claim 40, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

43. The method of claim 40, wherein the base is sodium hydroxide.

44. The method of claim 37, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

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45. The method of claim 44, wherein said natriuretic stabilizing compound is a protein or a polymer.

46. The method of claim 45, wherein the protein is bovine serum albumin,  
10 bovine gamma globulin, or a non-fat dry milk.

47. The method of claim 45, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

15 48. The method of claim 44, wherein the diluent further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

49. The method of claim 48, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

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50. The method of claim 48, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

51. The method of claim 48, wherein said base is sodium hydroxide.

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52. A stable test sample for use in a ligand binding assay for measuring the level of a natriuretic peptide in said test sample, wherein said test sample comprises a pH of from about 4.0 to about 6.5.

30 53. The test sample of claim 52, wherein said test sample comprises at least one human natural natriuretic peptide.

54. The test sample of claim 53, wherein said human natural natriuretic peptide is human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide or human natural *Dendroaspis* natriuretic peptide.

55. The test sample of claim 52, wherein said test sample comprises at least one diluent.

56. The test sample of claim 55, wherein said diluent has a pH of from about 4.0 to about 6.0.

57. The test sample of claim 56, wherein said diluent has a pH of from about 5.4 to about 5.6.

58. The test sample of claim 55, wherein said test sample comprises from about 5% to about 95% (v/v) of a diluent.

59. The test sample of claim 58, wherein said test sample comprises from about 20% to about 90% (v/v) of a diluent.

60. The test sample of claim 55, wherein said diluent comprises at least one natriuretic stabilizing compound.

61. The test sample of claim 60 wherein said natriuretic stabilizing compound is a protein or a polymer.

62. The test sample of claim 61, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

63. The test sample of claim 61, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

64. The test sample of claim 60, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

65. The test sample of claim 64, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

66. The test sample of claim 64, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

67. The test sample of claim 64, wherein the base is sodium hydroxide.

68. The test sample of claim 52, wherein said test sample can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

69. A stable test sample for use in a ligand binding assay for measuring the level of a natural natriuretic peptide in said test sample sample, wherein said test sample comprises:

from about 5% to about 95% (v/v) of at least one diluent; and

at least one biological sample derived from serum, plasma, whole blood or other bodily fluid that contains at least one natriuretic peptide,

wherein said test sample has a pH of from about 4.0 to about 6.5.

70. The test sample of claim 69, wherein said diluent has a pH of from about 5.0 to about 6.0.

71. The test sample of claim 70 wherein the diluent has a pH of from about 5.4 to about 5.6.



72. The test sample of claim 69, wherein the test sample comprises from about 20% to about 90% (v/v) of at least one diluent.

5 73. The test sample of claim 69, wherein the human natural natriuretic peptide is human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide or human natural *Dendroaspis* natriuretic peptide.

10 74. The test sample of claim 69, wherein said diluent comprises at least one natriuretic stabilizing compound.

75. The test sample of claim 74, wherein said natriuretic stabilizing compound is a protein or a polymer.

15 76. The test sample of claim 75, wherein the protein is bovine serum albumin, a bovine gamma globulin, or a non-fat dry milk.

20 77. The test sample of claim 75, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

78. The test sample of claim 69, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

25 79. The test sample of claim 78, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

30 80. The test sample of claim 78, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

81. The test sample of claim 78, wherein the base is sodium hydroxide.

82. The test sample of claim 69, wherein said test sample can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

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83. A method of making a stable, test sample for use in a ligand binding assay for measuring the level of a natriuretic peptide in said test sample, wherein the method comprises the step of:

10 mixing from about 5% to about 95% (v/v) of at least one diluent having a pH of from about 4.0 to about 6.0 with at least one biological sample derived from serum, plasma, whole blood or other bodily fluids and that contains at least one natriuretic peptide, to form a stable test sample having a pH from about 4.0 to about 6.5.

15 84. The method of claim 83, wherein the natural natriuretic peptide is human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide or human natural *Dendroaspis* natriuretic peptide.

85. The method of claim 83, wherein from about 70% to about 90% (v/v) of a diluent is mixed with at least one biological sample.

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86. The method of claim 83, wherein the diluent has a pH of from about 5.4 to about 5.6.

25 87. The method of claim 83, wherein said diluent comprises at least one natriuretic stabilizing compound.

88. The method of claim 87, wherein said natriuretic stabilizing compound is a protein or a polymer.

30 89. The method of claim 88, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

90. The method of claim 88, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

5 91. The method of claim 83, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

10 92. The method of claim 91, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

93. The method of claim 91, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

15 94. The method of claim 91, wherein said base is sodium hydroxide.

95. A method of stabilizing a test sample for use in a ligand binding assay for measuring the level of a natriuretic peptide in said test sample, wherein the method comprises the step of:

20 mixing from about 5% to about 95% (v/v) of at least one diluent having a pH of from about 4.0 to about 6.0 with at least one biological sample derived from serum, plasma, whole blood or other bodily fluids and that contains at least one natriuretic peptide, to form a stabilized test sample having a pH from about 4.0 to about 6.5.

25 96. The method of claim 95, wherein the natural natriuretic peptide is human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide or human natural *Dendroaspis* natriuretic peptide.

30 97. The method of claim 95, wherein from about 70% to about 90% (v/v) of a diluent is mixed with at least one biological sample.

98. The method of claim 95, wherein the diluent has a pH of from about 5.4 to about 5.6.

99. The method of claim 95, wherein said diluent comprises at least one  
5 natriuretic stabilizing compound.

100. The method of claim 99, wherein said natriuretic stabilizing compound is a protein or a polymer.

101. The method of claim 100, wherein the protein is bovine serum albumin,  
10 bovine gamma globulin, or a non-fat dry milk.

102. The method of claim 100, wherein the polymer is polyethylene glycol,  
dextran, dextran sulfate or polyvinyl pyrrolidone.

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103. The method of claim 95, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base .

20 104. The method of claim 103, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

105. The method of claim 103, wherein said acid is acetic acid, citric acid,  
diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

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106. The method of claim 103, wherein said base is sodium hydroxide.

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